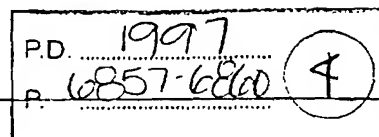


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Nonionic Bolaamphiphiles and Gemini Surfactants Based on Carbohydrates

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Introduction

Bolaamphiphiles (also known as bolaform surfactants, bolaphiles, or α,ω type surfactants) are molecules that have a hydrophilic group at both ends of a (long) hydrophobic chain.¹⁻³ Compared to the case for the single-headed amphiphiles, the introduction of a second head-group generally induces a higher solubility in water, an increase in the critical micelle concentration (cmc), and a decrease in the aggregation number.¹ The aggregate morphologies of bolaamphiphiles include spheres, large cylinders, small and large disks, and vesicles.¹

Gemini surfactants consist of two hydrophobic chains and two hydrophilic headgroups, linked by a relatively short (rigid or flexible) spacer.^{4,5} The gemini surfactants reported thus far all possess ionic headgroups.⁶ This class of compounds shows intriguing properties, including higher cmc's for geminis with two long chains (16-20 carbon atoms) than for the shorter chain analogs, submicellar aggregation, markedly low surface tensions, good oil solubilization properties, and the formation of thread-like micelles.⁴⁻¹⁰

The interest in nonionic bolaamphiphiles based on carbohydrates is increasing.¹¹⁻¹⁸ Recently, patents on

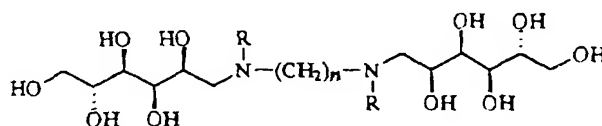


Figure 1. Structures of bis(1-amino-1-deoxy-D-glucityl)alkanes (1, R = H; 1a, $n = 6$; 1b, $n = 8$; 1c, $n = 10$) and bis(*N*-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes (2, R = C(=O)-C₁₃H₂₇; 2a, $n = 6$; 2b, $n = 8$; 2c, $n = 10$).

carbohydrate-based gemini surfactants have been granted,^{19,20} but to our knowledge, nonionic (carbohydrate-based) geminis have not been reported in the open literature.⁶ Herein we report novel nonionic bolaamphiphiles 1, prepared directly from D-glucose, and α,ω -diaminoalkanes and nonionic gemini surfactants 2, obtained by acylation of 1 (Figure 1). A preliminary study of their aggregation behavior has been made.

Experimental Section

Materials. Starting materials and solvents were purchased from any of the large chemical suppliers.

Characterization. ¹H- and ¹³C-NMR spectra were run on a Varian VXR 300 spectrometer at 50 °C. Melting points, Krafft temperatures, and the corresponding enthalpies were determined by differential scanning calorimetry on a Perkin Elmer DSC7 PC Series apparatus (heating/cooling rates 5 K min⁻¹). The lyotropic mesophase textures were studied by polarizing optical microscopy using a Nikon polarizing microscope equipped with a Mettler FP82 hot stage (linked to a Mettler FP80 temperature controller) and a Minolta 7000 camera.

Vesicle Preparation. Vesicles were prepared either with a Branson cell disruptor (2 min, 40 W, pulsed, 55 °C) or with an MSE sonicator (6 cycles of 20 s sonication with a 5 s rest period in between, amplitude 19 μ m). Solutions (5 mM) were prepared (5 mL) and sonicated for 2 min. A 25 mM aqueous solution of sodium dodecylbenzenesulfonate (50 μ L) was added, and the solution was sonicated again for 2 min.

Electron Microscopy. Aliquots of solutions of 2a-2c were applied on carbon-coated formvar grids, negatively stained with a 2% (w/v) solution of sodium phosphotungstate (PTA, pH 7.2), and examined in a Philips 201 electron microscope (operating at 100 kV). For cryo electron microscopy, aliquots of 2a and 2c were absorbed onto holey carbon grids which were plunged into liquid ethane and then observed in a Philips CM120 electron microscope at about -170 °C using a Catan 626 cryo holder. Observations were made under low dose conditions, at 120 kV.

Bis(1-amino-1-deoxy-D-glucityl)alkanes (1). These bolaamphiphiles were prepared in yields up to 75% by catalytic hydrogenation at elevated pressure (40 bar, 40 °C, 24 h) of 2 mol equiv of D-glucose and the appropriate α,ω -diaminoalkane in the presence of 5% palladium on carbon. The products could be crystallized from their reaction mixtures (methanol/water) after the Pd/C had been filtered off.

Bis(1-amino-1-deoxy-D-glucityl)hexane (1a). ¹H NMR (DMSO-*d*₆, ppm): 1.14 (m, 4H), 1.26 (m, 4H), 2.36 (m, 8H), 3.39

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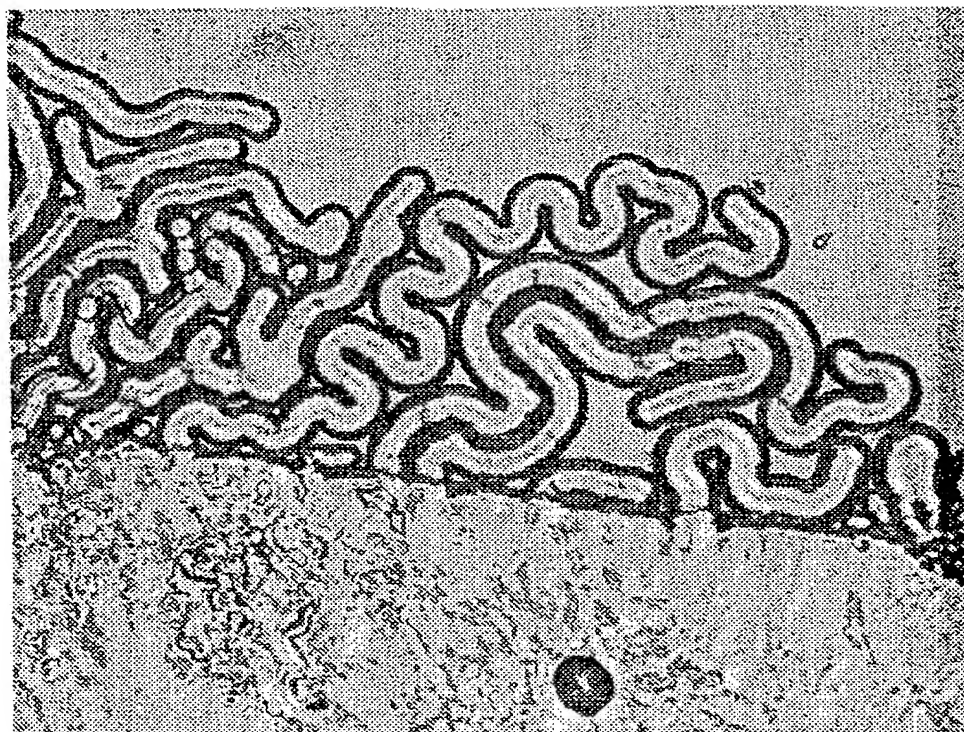


Figure 2. Formation of lyotropic mesophases in a contact preparation of water and 2c, 45 °C: from top to bottom, water–myelin figures–L₄.

(m, 12H), 3.51 (m, 8H). ¹³C-NMR (DMSO-*d*₆, ppm): 26.66, 29.31 (C₂, C₃), 49.17, 50.97 (C₁, C₁'), 63.67 (C₆), 70.76, 70.86, 71.12, 71.36 (C₂–C₅).

Anal. Calcd for C₁₈H₃₂N₂O₁₀: C, 48.64; H, 9.07; N, 6.30. Found: C, 48.68; H, 8.99; N, 6.31.

Bis(1-amino-1-deoxy-D-glucityl)octane (1b). Anal. Calcd for C₂₀H₃₄N₂O₁₀: C, 50.83; H, 9.38; N, 5.93. Found: C, 50.88; H, 9.35; N, 5.84.

Bis(1-amino-1-deoxy-D-glucityl)decane (1c). Anal. Calcd for C₂₂H₃₈N₂O₁₀: C, 52.78; H, 9.66; N, 5.60. Found: C, 52.55; H, 9.39; N, 5.48.

Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)-alkanes (2). The corresponding geminis (2a–c, Figure 1) were obtained by acylation of the bolaamphiphiles with a small excess of tetradecanoic anhydride in ethanol. The solution was neutralized with Dowex OH[−] (Sigma). The products were crystallized from ethanol (2a, 65%) or ethylacetate (2b, 73%) or were extracted with hexane (2c, 78%, to remove excess fatty acid).

Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)hexane (2a). ¹H-NMR (CD₃OD, ppm): alkyl chain 0.97 (t, 6H), 1.37 (s, 4H), 1.67 (m, 8H), 2.18 (dt, 4H), sugar moiety 3.56 (m, 18H), 4.04 (m, 2H), 4.73 (s, 10H). ¹³C-NMR (CD₃OD, ppm): 14.66 (C₁₁'), 23.92, 26.91, 27.01, 27.81, 27.89, 28.45, 30.04, 30.65, 30.77, 30.85, 30.98, 33.28, 34.33, 34.60 (C₂, C₃, C₂', C₁₃'), 47.65, 51.02, 51.99 (C₁, C₁'), 65.10 (C₆), 71.67, 72.03, 73.11, 73.43, 73.55, 73.63, 74.10, 74.57 (C₂, C₅), 176.67, 176.79, 176.85 (C₁'). Note: double or triple resonances are due to the presence of rotamers caused by the amide bonds. Anal. Calcd for C₁₆H₃₂N₂O₁₂: C, 63.89; H, 10.72; N, 3.24. Found: C, 63.56; H, 10.55; N, 3.32.

Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)-octane (2b). Anal. Calcd for C₁₈H₃₆N₂O₁₂: C, 64.54; H, 10.83; N, 3.14. Found: C, 64.57; H, 10.79; N, 3.21.

Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)-decane (2c). Anal. Calcd for C₂₀H₄₀N₂O₁₂: C, 65.18; H, 10.91; N, 3.04. Found: C, 65.60; H, 10.75; N, 3.07. Due to problems with the crystallization no fully satisfactory analysis could be obtained.

Results and Discussion

The aggregation behavior of the bolaamphiphiles and the gemini surfactants was studied by means of the contact

Table 1. Physical Properties of Bis(1-amino-1-deoxy-D-glucityl)alkanes (1) and Bis(N-tetradecanoyl-1-amino-1-deoxy-D-glucityl)alkanes (2)

compd	mp (°C)	Δ <i>H</i> _{melt} (kJ·mol ^{−1})	<i>T</i> _{Krafft} ^a (°C)	Δ <i>H</i> _{Krafft} (kJ·mol ^{−1})
1a	151.4–153.4	112.8	53	28.0
1b	151.9–154.2	116.0	74	55.0
1c	150.0–152.0	116.5	90	81.4
2a	76.8–82.2 ^b	57.4	32	45.5
2b	94.4–96.0 ^c	83.7	43	63.7
2c	83.1–87.6	63.9	38	50.7

^a Broad transition. ^b Clearing point, 135.2 °C (smectic A phase).²⁵

^c Monotropic smectic A; clearing point upon cooling, 11.5 °C.²⁵

preparation method. When water penetrates an amphiphilic sample, one or more lyotropic mesophases are often formed as bands around the anhydrous bulk of the sample, and consequently the entire concentration range from pure water to anhydrous compound is present.²¹ These lyotropic mesophases are an indication of the kind of aggregates formed when the compound is dissolved in water. Unfortunately, the bolaamphiphiles 1a–1c dissolve in water only at high temperatures and do not form lyotropic mesophases. The gemini surfactants, on the other hand, show intriguing properties upon hydration. Gemini 2c displays myelin formation in the temperature range from 45 °C to about 65 °C (Figure 2), which suggests that vesicles will be formed in dilute solution.^{21,22} By contrast, geminis 2a and 2b show cubic and lamellar phases, the latter being observed at higher surfactant concentrations.

The Krafft temperature of a surfactant may be viewed as its melting point in an aqueous environment.²² In the solid state, the hydrogen bonds and the London dispersion forces are much stronger in the tightly packed linear

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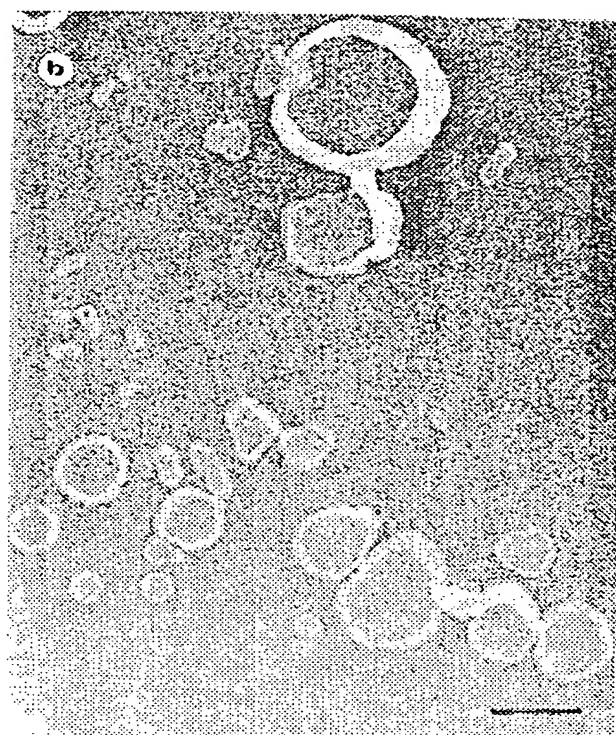
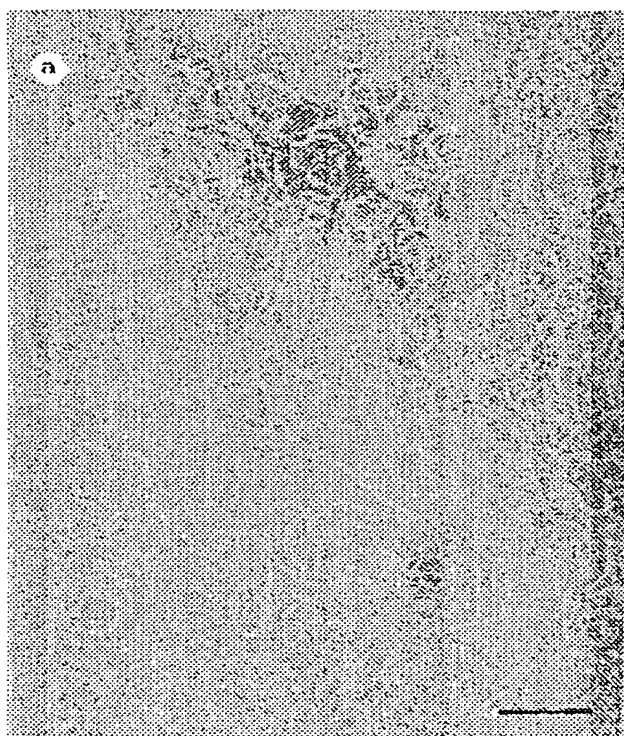


Figure 3. Negatively stained (2% PTA) electron micrographs of (a) **2a** (presence of threadlike micelles) and (b) vesicles formed by **2c**. The bars represent 100 nm.

bolaamphiphiles than in the gemini surfactants, where close packing is hampered by the presence of two bulky acyl side chains. This results in lower Krafft temperatures as well as in lower melting points (and melting enthalpies) for the gemini surfactants (Table 1). For the bolaamphiphiles, the spacer length has little influence on the melting points and the enthalpy of melting, this suggests that the packing of these compounds in the solid state is similar and determined predominantly by the carboxylate headgroup.¹⁷

Solutions of the geminis were prepared by sonicating

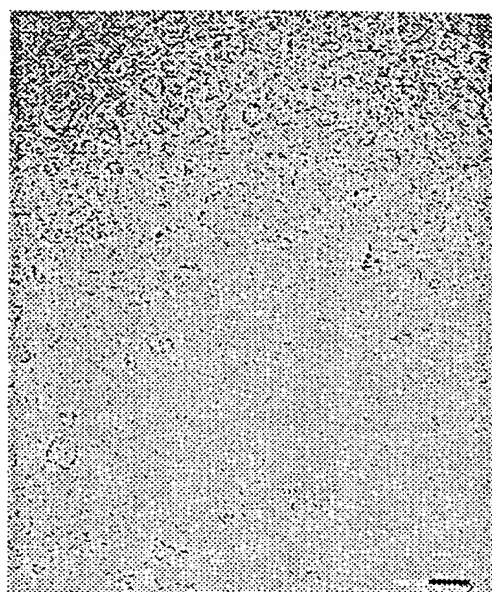


Figure 4. Cryo-transmission electron micrograph showing sheets, vesicles, and threadlike micelles formed by **2a**. The bar represents 100 nm.

5 mM turbid solutions of compounds **2a–2c** at 55 °C; it was necessary to add 5 mol % of an anionic surfactant (sodium dodecylbenzenesulfonate) to increase the solubility of the gemini surfactants. Electron microscopy confirmed that the length of the spacer of the gemini surfactants has a dramatic influence on the morphology of the aggregates formed. Electron micrographs of negatively stained samples (Figure 3) show that **2c**, with a spacer length of ten methylene groups, forms vesicles (as predicted), whereas compounds **2a** and **2b** with spacer lengths of six and eight methylene groups, respectively, display threadlike micelles (Figure 3a). Since negative staining is known to give rise to staining and drying artifacts,²³ we also performed cryoelectron microscopy experiments on compounds **2a** and **2c** which provide a more realistic view of the samples under investigation.²⁴ For **2c** again vesicles were observed. Compound **2a** displayed sheets and both vesicles and threadlike micelles (Figure 4). We simultaneously observed that the solution of **2a** is clear when prepared at 55 °C and then becomes bluish after 0.5 h in an oven at 60 °C and turns clear again when cooled down to room temperature. The ultimate clear solution is viscoelastic and much more viscous than water (the initial clear solution is *not* viscoelastic). We contend that this viscoelasticity is due to the conversion of vesicles into threadlike micelles. The clear, viscous solution remains stable for about 1 day. The solution prepared from **2b** is bluish at room temperature and becomes clear and viscoelastic when placed in the refrigerator. For both compounds, this process is reversible. The solution of **2c** remains bluish at all temperatures, is not viscous, and does not display viscoelastic behavior. This indicates that the vesicles formed by the gemini surfactants become more stable when the spacer length is increased.

Conclusions

A series of nonionic bolaamphiphiles and gemini surfactants was synthesized. The gemini surfactants show interesting aggregation behavior. When the spacer length

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is decreased from 10 to 6 methylene groups, the vesicles formed by these surfactants become less stable and turn into threadlike micelles upon cooling, thus giving the solution a viscous and viscoelastic character. This process is reversible.

Notes

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